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09/937,008	05/06/2002	Lieven De Veylder	2364/400	2821

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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,008	DE VEYLDER ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1--41* is/are pending in the application.

4a) Of the above claim(s) *3-12 and 15-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,13,14 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0502*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group XII, claims 1-2, 13-14 and 31, drawn to a method for modifying plant growth and/or yield or modifying architecture using (a) nucleic acid molecule(s) or regulatory sequence(s) that result in increased de novo expression of at least two cell cycle interacting proteins, wherein one of said cell cycle interacting proteins is an E2F protein, and to a composition, filed February 2, 2004, is acknowledged.

The traversal is on the ground(s) that there is one single general inventive concept which specifically describes the unique special technical feature of each group, which involves the co-expression of at least two genes coding for cell cycle interacting proteins that form a complex useful in a method for modifying plant growth and/or yield and/or architecture, which is not disclosed or suggested in the prior art (reply pages 3-4).

This is not found persuasive because the co-expression of at least two genes coding for cell cycle interacting proteins that form a complex useful in a method for modifying plant growth and/or yield and/or architecture is obvious in view of the prior art, as set forth below in the rejection under 35 USC 103.

The traversal is on also the ground(s) that non-unity objections were not raised in the International Preliminary Examination Report (reply page 4).

This is not found persuasive because the failure to raise non-unity objections in the International Preliminary Examination Report does not preclude raising non-unity objections in the instant application, especially in view of the multiple references in the prior art directed to the co-expression of different cell cycle interacting proteins in animal cells, and the multiple

references in the prior art directed to the conservation of structure and function of cell cycle interacting proteins in all eukaryotic organisms, including plants.

The traversal is on also the ground(s) that the art cited in the restriction requirement mailed December 30, 2003 does not anticipate or render obvious the claimed invention. In particular, Applicant argues that the cited patent (US 5,514,571) is non-analogous, as the experiments were performed in animal cells rather than plant cells, and that the cited references (Hemerly et al. and Riou-Khamlichi et al.), would not motivate one skilled in the art to co-express two genes coding for cell cycle interacting proteins that form a complex for the purpose of modifying plant growth and/or yield and/or architecture (reply pages 4-7).

This is not found persuasive because the co-expression in animal cells of at least two genes coding for cell cycle interacting proteins that form a complex is considered to be analogous art, since the prior art teaches the conservation of the structure and function of cell cycle interacting proteins in all eukaryotic organisms, including plants, and the claims require only the expression in a plant cell, tissue or plant of these proteins, without reference to the production of any specific effect. This is also not found persuasive because the co-expression of at least two genes coding for cell cycle interacting proteins that form a complex useful in a method for modifying plant growth and/or yield and/or architecture is obvious in view of the prior art, as set forth below in the rejection under 35 USC 103.

The traversal is on also the ground(s) that it is in the public interest to permit applicants to claim several aspects of their invention together in one application, as Applicant has done here (reply pages 7-9).

This is not found persuasive because the different groups of invention set forth in the restriction requirement mailed December 30, 2003 are not considered to be different aspects of a single invention. The different groups of invention set forth in the restriction requirement mailed December 30, 2003 require the use of structurally and functionally distinct proteins encoded by structurally and functionally distinct genes that are differentially expressed and that perform distinct roles in the regulation of the cell cycle, and for these reasons the different groups of invention are considered to be patentably distinct.

Accordingly, claims 3-12, 15-30 and 32-41 are withdrawn from consideration as being directed to non-elected inventions. The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, filed May 6, 2002, is attached to the instant Office action.

Specification

The disclosure is objected to because of the following informalities: The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.Appropriate correction is required.

Claim Objections

Claims 1-2, 13-14 and 31 are objected to because of the following informalities: claims 1-2 and 31 are not directed to the elected cell cycle interacting protein, and claims 13-14 recite non-elected cell cycle interacting proteins. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-2 are drawn to a method for modifying plant growth and/or yield or modifying architecture by introducing into a plant cell, tissue or plant nucleic acid molecule(s) of undefined structure, including molecules that code for unidentified cell cycle interacting proteins, or regulatory sequence(s) of undefined structure, including sequences capable of increasing the expression of genes encoding unidentified cell cycle interacting proteins, wherein the introduction of said molecule(s) or sequence(s) results in increased or de novo expression of at least two unidentified cell cycle interacting proteins capable of forming a (heteromeric) complex in a plant cell. Claim 31 is drawn to a composition comprising vectors wherein each vector

contains at least one nucleic acid molecule encoding at least one unidentified cell cycle interacting protein capable of forming a (heteromeric) complex in a plant cell, wherein expression of said vectors results in the production of at least two unidentified cell cycle interacting proteins and assembly of the same in a complex in vitro or in vivo.

The specification describes the cell cycle interacting proteins of the instant invention as generally being any protein which in any way controls or regulates is required for the cell cycle or a part thereof (page 13 3rd paragraph), and makes particular reference to certain proteins associated with the cell cycle that are known to interact by forming heteromeric complexes, such as cyclin and cyclin-dependent kinase proteins, ORC1 and CDC6 proteins, CDC7 and DBF4 proteins, and E2F and DP proteins (pages 2-4, pages 62-63). The specification does not describe other types of cell cycle proteins that are known to interact by forming heteromeric complexes, or the sequences that encode them, or plant cells, tissues or plants into which such sequences have been introduced and expressed. The specification also does not describe any regulatory sequences capable of increasing the expression of genes encoding cell cycle interacting proteins, or plant cells, tissues or plants into which such sequences have been introduced and expressed.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that "A description of a genus of cDNAs may be achieved by means of recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1569; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In the instant case Applicant has not described a representative number of species falling within the

scope of the claimed genus of sequences that would, when introduced into a plant cell, tissue or plant, result in increased or de novo expression of any and all combinations of cell cycle interacting proteins capable of forming a (heteromeric) complex in a plant cell, nor the structural features unique to the genus.

Claims 1-2, 13-14 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-2 are drawn to a method for modifying plant growth and/or yield or modifying architecture by introducing into a plant cell, tissue or plant nucleic acid molecule(s) of undefined structure, including molecules that code for unidentified cell cycle interacting proteins, or regulatory sequence(s) of undefined structure, including sequences capable of increasing the expression of genes encoding unidentified cell cycle interacting proteins, wherein the introduction of said molecule(s) or sequence(s) results in increased or de novo expression of at least two unidentified cell cycle interacting proteins capable of forming a (heteromeric) complex in a plant cell. Claim 13 is drawn to the method of claim 1 or 2 wherein one cell cycle interacting protein is E2F, and claim 14 is drawn to the method of claim 13 wherein one cell cycle interacting protein is E2F and the other is DP. Claim 31 is drawn to a composition comprising vectors wherein each vector contains at least one nucleic acid molecule encoding at least one unidentified cell cycle interacting protein capable of forming a (heteromeric) complex in a plant

cell, wherein expression of said vectors results in the production of at least unidentified two cell cycle interacting proteins and assembly of the same in a complex in vitro or in vivo.

The specification discloses that the cell cycle interacting proteins of the instant invention generally include any protein which in any way controls or regulates is required for the cell cycle or a part thereof (page 13 3rd paragraph), and preferably include proteins involved in the control of entry and progression through the S phase, such as an E2F protein (page 14 3rd paragraph). With respect to the elected invention, the specification does not disclose any specific E2F proteins or the sequences that encode them, or the effect of expressing such sequences in plant cells, tissues or plants into which such sequences have been introduced. The specification also does not disclose the identity of proteins other than DP that would interact with an E2F protein to form a heteromeric complex. Additionally, the specification does not disclose any regulatory sequences capable of increasing the expression of genes encoding cell cycle interacting proteins, or plant cells, tissues or plants into which such sequences have been introduced and expressed.

The disclosure is not enabling for the claimed invention because it does not provide sufficient guidance for one skilled in the art to determine how to specifically modify some defined aspect(s) of plant growth and/or yield or architecture by introducing into a plant cell, tissue or plant nucleic acid molecule(s) that code for or that regulate the expression of an E2F cell cycle interacting protein. Such guidance is necessary because it is unpredictable what specific effect increased or de novo expression of an E2F protein would have on plant growth and/or yield or architecture, because different aspects of plant growth and development are affected by cell division in different ways, and because expressing different types of E2F proteins can have different effects on the cell cycle.

See for example den Boer et al. (Current Opinion in Biotechnology, 2000, Vol. 11, pages 138-145), who teach that cell division is known to be fundamental to plant development, and that manipulating when and where cell division occurs could provide the opportunity to change plant architecture, growth rate and yield, provided that cell division can be controlled in a way that is correctly integrated with plant development, which to be achieved will require a greater understanding of processes such as how cell cycle factors regulate cell cycle progression, how gene networks contribute to the formation of organ structures, what makes cells exit the cell cycle, and how cell growth and division are connected (page 138 column 2 second and third full paragraphs). De Boer et al. also teach that expressing different types of cell cycle interacting proteins in transgenic plants has been shown to result in different types of specific effects on plant growth and development (page 141 Table 1). See also for example Mann et al. (Curr Biol. 1996 Apr 1;6(4):474-83), who teach that expression of the human E2F-1 protein in U2-OS cells overcomes p16 mediated G1 arrest, whereas expression of the human E2F-4 protein does not (page 478 Figure 4). Mann et al. also teach that the functional difference between the E2F-1 protein and the E2F-4 protein are dependent on amino-terminal regions that contain E2F DNA-binding and dimerization domains, indicating that these two different E2F proteins are likely to regulate the expression of different sets of genes (page 474 abstract; page 479 Figure 5; page 482 column 1 first paragraph).

Given the unpredictability of the effect that increased or de novo expression of an E2F protein would have on plant growth and/or yield or architecture, and given the lack of guidance in the disclosure and in the prior art, it would require undue experimentation for one skilled in the art to determine how to increase or initiate E2F protein expression in a plant cell, tissue or

plant in a way that would specifically modify plant growth and/or yield or architecture, as one skilled in the art would have to resort to trial and error experimentation in order to determine which E2F protein to express, as well as when, where, and how much to express it, in order to achieve a particular result.

The disclosure also is not enabling for the claimed invention because it does not provide sufficient guidance for one skilled in the art to determine which proteins other than DP would interact with an E2F protein to form a heteromeric complex, and which regulatory sequences would be capable of increasing the expression of genes encoding E2F. Such guidance is necessary because one skilled in the art needs access to the materials necessary to practice the claimed invention, and such materials do not appear to be accessible in the prior art. Neither the prior art of record nor the disclosure indicate the identity of proteins other than DP that would interact with an E2F protein to form a heteromeric complex that one skilled in the art could use to practice the claimed invention, or the identity of regulatory sequences that would be capable of increasing the expression of genes encoding E2F that one skilled in the art could use to practice the claimed invention.

Given that the rejected claims encompass the use of nucleic acid molecules that code for any and all cell cycle interacting proteins that are capable of forming a heteromeric complex with E2F, or regulatory sequences that function in any way to regulate the expression of E2F or the expression of any and all cell cycle interacting proteins that are capable of forming a heteromeric complex with E2F, and given the lack of guidance in the disclosure and in the prior art, it would require undue experimentation for one skilled in the art to determine which nucleic acid molecules or regulatory sequences to use and how to use them, as one skilled in the art would

have to resort to trial and error experimentation in order to identify and clone the desired nucleic acid molecules and regulatory sequences, as well as to test their specific effect on plant growth and/or yield or architecture.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 31 is rejected under 35 U.S.C. 102(b) as being anticipated by Lathangue (WO 97/02354, International Publication Date 23 January 1997, Applicant's IDS).

Claim 31 is drawn to a composition comprising vectors wherein each vector contains at least one nucleic acid molecule encoding at least one cell cycle interacting protein capable of forming a (heteromeric) complex in a plant cell, wherein expression of said vectors results in the production of at least two cell cycle interacting proteins and assembly of the same in a complex in vitro or in vivo.

Lathangue teaches a host cell composition comprising vectors wherein each vector contains at least one nucleic acid molecule encoding a p53 protein and one or both of a DP protein and an E2F protein (page 29 claim 1, page 30 claim 14). The encoded proteins are inherently capable forming a (heteromeric) complex in a plant cell, and would inherently assemble in a complex in vitro or in vivo, as DP and E2F are known to form heterodimers, and p53 is known to interact with DP, in eukaryotic cells (page 2 lines 5-15 and lines 28-32).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2 and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lukas et al. (Molecular and Cellular Biology, March 1996, pages 1047-1057) in view of Huntley et al. (Plant Molecular Biology, May 1998, Vol. 37, No. 1, pages 155-169).

The claims are drawn to a method for modifying plant growth and/or yield or modifying architecture by introducing into a plant cell, tissue or plant nucleic acid molecule(s), including molecules that code for cell cycle interacting proteins that include E2F and DP, wherein the introduction of said molecule(s) results in increased or de novo expression of at least two cell cycle interacting proteins capable of forming a (heteromeric) complex in a plant cell.

Lukas et al. teach a method of modifying animal cell growth by introducing into rat fibroblast cells nucleic acid molecules that code for E2F and DP cell cycle interacting proteins, wherein expression of DP-1 with E2F-4 or E2F-5 promoted S-phase entry and accelerated G1 progression, as compared to rat fibroblast cells transfected with DP-1 alone or with E2F-4 or E2F-5 alone (page 1054 Figure 5 B and C). Lukas et al. also teach that E2F and DP are known to form functional heterodimers that are essential for high-affinity DNA binding, transcriptional activity, and binding to pocket proteins (page 1048 column 1 first paragraph).

Lukas et al. do not teach a method for modifying plant growth and/or yield or architecture.

Huntley et al. teach that the maize plant retinoblastoma protein ZmRb-1 can bind human and Drosphila E2F proteins, and can suppress human E2F-activated transcription in human U2OS cells (page 163 Figure 4 (C)), indicating structural and functional conservation of proteins involved in G1/S transition in the cell cycle in plants and animals.

Given the success of Lukas et al. in promoting S-phase entry and accelerating G1 progression by increasing the expression of E2F and DP cell cycle interacting proteins in an animal cell, and given the teachings of Huntley et al. that the proteins involved in G1/S transition in plants and animals are structurally and functionally conserved, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to express E2F and DP cell cycle interacting proteins such as those taught by Lukas et al. in a plant cell. One would have been motivated to do so because the general correlation between cell division and plant growth and development was well-known in the art at the time of filing, and because the claims do not require that any specific modification of plant growth and/or yield or architecture result from the increased or de novo expression. One would also have a reasonable expectation of success, since increasing the expression of recombinant proteins in plant cells, tissues and plants was routine in the art at the time of filing. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins  4/30/04